REMARKS

Entry of the foregoing and further and favorable consideration of the subject application are respectfully requested and such action is earnestly solicited.

As correctly stated in the Official Action, Claims 1-17, 20, 21, and 23-30 are pending in the present application. Claims 11-17, 20, 23-25, and 27-29 stand withdrawn from consideration.

By the present amendment, Claim 1 has been amended to recite "wherein said target cell is a mammalian cell." Support for this amendment can be found, at least, on page 5, lines 14-17 and page 13, line 11, of the specification. Claims 1 and 7 have been amended to correct minor typographical errors. No new matter has been added.

Request for Withdrawal of the Finality of Official Action

Applicants respectfully request that the finality of the present Official Action be withdrawn. The present Official Action comprises new rejections over newly cited prior art.

According to M.P.E.P. §706.07(a), "[a] second or any subsequent action on the merits in any application ... should not be made final if it includes a rejection, on prior art not of record, of any claim amended to include limitations which should reasonably have been expected to be claimed." In response to the previous Office Action, the claims were amended to recite genes of therapeutic interest which are clearly disclosed in the examples

of the instant application. Applicants respectfully submit that such a limitation should have reasonably been expected by the Examiner.

Accordingly, the Official Action is not properly a final action. Withdrawal of the finality of the outstanding Official Action is respectfully requested.

Rejections Under 35 U.S.C. § 102

Claims 1-3 and 30 stand **newly** rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Wittup et al. (USPN 6,423,538). This rejection is respectfully traversed.

According to the Official Action, Wittrup et al. allegedly disclose a DNA plasmid vector comprising a gene of interest and a Gal promoter and regulatory sequence such as f1(+) origin, wherein the gene of interest is a single chain anti-TCR antibody KJ16.

The disclosure of Wittrup et al. is dedicated to the expression of a polypeptide by yeast. *See* Abstract. More particularly, the expressed polypeptide is linked to the yeast cell wall. *See* Col. 3, l. 63 and Figure 2. In this respect, the disclosed DNA plasmid vector comprises a promoter sequence, the gal promoter (*see* Figure 3), which is specific to yeast, and an anchoring protein, Aga1 (*see* Figure 2 and Col. 13, ll. 24-29), which is able to interact specifically to the yeast cell wall.

To the contrary, the presently claimed invention discloses a nucleic acid sequence containing at least one gene encoding all or part of an antibody which will be **expressed at the surface of a target cell**. The present application clearly states that the target cells are mammalian target cells, and more particularly, tumor cells or cells infected by a pathogenic

agent. *See, e.g.*, p. 5, ll. 14-17 and p. 13, l. 11). It is well-known that mammalian cells do not have a cell wall like yeast but only a cell membrane made up of a lipid bilayer. Therefore, the transfection of the nucleic acid disclosed by Wittrup et al. in a mammalian cell would not lead to the expression of a polypeptide at the surface of this cell. Moreover, as the nucleic acid of Wittrup et al. comprises a promoter which is specific to yeast, it would not be transcribed in a mammalian cell.

Applicants note that by the present amendment, Claim 1 recites, "wherein the target cell is a mammalian cell." To anticipate a claim under 35 U.S.C. § 102, a reference must disclose or suggest each and every element of the presently claimed invention. Wittrup et al. do not disclose or suggest each and every element of the presently claimed invention and cannot be anticipatory. Withdrawal of this rejection is respectfully requested.

Claims 1-3 and 30 stand **newly** rejected under 35 U.S.C. § 102(a) and (e) as purportedly anticipated by Burkly et al. (USPN 5,871,732) as evidenced by Janeway, Jr. et al. (*Immunobiol.* 1999). This rejection is respectfully traversed.

According to the Official Action, Burkly et al. allegedly disclose a DNA plasmid vector encoding a humanized anti-CD4 antibody linked to a promoter and regulatory sequence for expressing the recombinant antibody. The Office Action purports that CD4 is a T cell receptor comprising TCR-α and TCR-β. Applicants respectfully submit that this is **incorrect**. Moreover, it is not apparent where in the Janeway publication it is disclosed

that CD4 comprises TCR-α and TCR-β. CD4 is a single chain glycoprotein. *See, e.g.*, Cruse et al., Illustrated Dictionary of Immunology, p. 54, attached hereto as Exhibit A.

Accordingly, Burkly et al. do not disclose or suggest each and every element of the presently claimed invention. Withdrawal of this rejection is respectfully requested.

Claims 1-6, 21, 26, and 30 stand **newly** rejected under 35 U.S.C. § 102(e) as allegedly anticipated by German et al. (USPN 6,531,455). This rejection is respectfully traversed.

According to the Official Action, German et al. disclose a nucleic acid sequence comprising a gene of interest and a promoter and regulatory sequence wherein the preferred gene of interest is an anti-CD3.

Applicants respectfully submit that German et al. disclose methods for **delivering a polypeptide to the bloodstream** of a subject by the introduction of a nucleic acid construct into secretory gland cells. *See* Abstract. Therefore, the nucleic acid disclosed by German et al. comprises a gene coding for a soluble protein, which does not comprise a region which allows the anchoring to the cell membrane. In this respect, the compositions used by German et al. are completely different from the presently claimed invention which allows the expression of an antibody **at the surface of the target cell**. As disclosed on page 7 of the application, the term "at the surface of the target cell" means that the antibodies according to the invention comprise an amino acid sequence which allows the

anchoring within the membrane bilayer of the target cell, or at the external surface of the target cell. *See* p. 7, ll. 18-21.

Accordingly, German et al. do not disclose or suggest each and every element of the presently claimed invention. Withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. § 103

Claims 1-10, 21, 26, and 30 stand **newly** rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Dixit et al. (USPN 6,562,797) in view of Schneck et al. (USPN 6,448,071) and Wittrup et al. This rejection is respectfully traversed.

According to the Official Action, Dixit et al. allegedly disclose delivering a nucleic acid construct encoding FADD polypeptide to a mammal, and, for the purpose of T cell targeting, a T cell specific ligand such as an anti-CD3 antibody. As depicted in Figure 8, FADD can interact with the intracytoplasmic death domain of Fas. Therefore, Dixit et al. disclose a molecule which is expressed **inside** the target cell **not at the surface**.

As discussed above, Wittrup et al. purportedly disclose a DNA plasmid vector comprising a gene of interest and a Gal promoter and regulatory sequence such as f1(+) origin, wherein the gene of interest is a single chain anti-TCR antibody KJ16 which can only be expressed **at the surface of a yeast cell, not at the surface of a mammalian cell**.

According to the Office Action, Schneck et al. disclose the need in the art for studying the selective interaction of T cell receptors with their cognate ligand and using a nucleic acid sequence encoding MHC Class II or TCR heterodimers linked with murine

antibody heavy and light chains in a baculovirus expression system, wherein the expression system comprises promoters and enhancers that would ensure the expression of the gene of interest *in vivo* in a target cell, wherein said nucleic acid sequence could be in the form of a naked polynucleotide or a vector, **wherein the heavy and light chain of the antibody is fused with a transmembrane polypeptide (Claims 1 and 9, Col. 5, ll. 40-41)**, wherein the transmembrane polypeptide is a glycoprotein TCR α/β chain. Applicants respectfully submit that this is incorrect. Claims 1 and 9 disclose the use of the **extracellular domain** of a transmembrane polypeptide, not the use of a transmembrane domain of a transmembrane polypeptide. Col. 5, ll. 40-41 do not refer to a transmembrane polypeptide. To the contrary, this passage refers to Figure 2, which discloses an expression vector encoding **soluble** divalent heterodimeric proteins. *See* title of Figure 2.

Applicants respectfully submit that the Examiner has misunderstood the disclosure of Schneck et al. regarding the function of the transmembrane polypeptide and of the heavy and light chain of the antibody. The goal of Schneck et al. is to produce a **soluble form** of a polypeptide deriving from heterodimeric double transmembrane protein such as TCR or Class II MHC. *See* Col. 5, ll. 27-49. To this end, the sequences encoding the signal sequence and **extracellular domain** of one polypeptide of the heterodimeric complex are fused to the first amino acid of either the heavy or light chain immunoglobulin variable region. *See* Col. 12, ll. 19-25. The resulting polypeptides are depicted in Figure 1C and 1D. In this regard, the antigen binding site of the antibody is not functional as it has been

modified by mutation in order to be linked to the extracellular domain of one polypeptide of the heterodimeric complex. *See* Col. 20, ll. 24-27.

In contrast, the presently claimed invention discloses nucleic acid sequences coding for antibodies which will be **expressed at the surface of a target cell** (*i.e.*, that are linked to the membrane of the cell) and wherein said antibodies are able to bind to the TCR complex. Therefore, our invention is totally different from the disclosure of Schneck et al. which discloses nucleic acids encoding for divalent proteins which:

- are not expressed at the surface of the target cell, but are in a soluble form in the supernatant of the target cells (*see* Col. 21, ll. 49-50); and

- do not comprise an antigen binding site.

The genetic construct taught by Schneck et al. is only dedicated to heterodimeric double transmembrane protein. Thus, it would not have been possible to combine the disclose of Schneck et al. with the disclosure of Dixit et al. or of Wittrup et al. because FADD and KJ16 are single chain monomeric molecules. Moreover, even assuming *arguendo* that one skilled in the art could and did combine these disclosures, he would have obtained a soluble polypeptide, not a polypeptide expressed at the surface of the target cells.

Thus, none of the cited publications, either alone or in combination, discloses or suggests every element of the presently claimed invention. Additionally, as discussed above, it is impossible to combine the cited publications and one skilled in the art would

not be motivated to do so. Accordingly, the cited publications cannot render the presently claimed invention obvious. Withdrawal of this rejection is respectfully requested.

Conclusions

From the foregoing, further and favorable consideration of the subject application on the merits is respectfully requested and such action is earnestly solicited.

If there are any questions concerning this amendment, or the application in general, the Examiner is respectfully requested to telephone Applicant's undersigned representative so that prosecution may be expedited.

Respectfully submitted,

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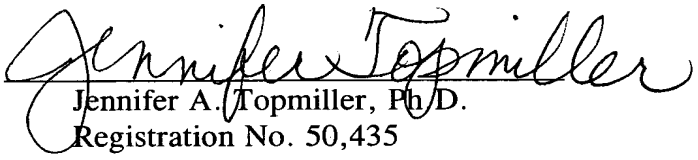
By: 
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